IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Attorney Docket No. 2006_1312A
Hiide YOSHINO et al.	:	**Confirmation No. 4646**
Serial No. 10/588,778	:	Group Art Unit 1612
Filed December 3, 2007	:	Examiner Marcos L. Sznaidman
A NOVEL THERAPEUTIC AGENT FOR AMYOTROPHIC LATERAL SCLEROSIS (ALS) OR DISEASES CAUSED BY ALS	:	**Mail Stop: AMENDMENT**

SUBMISSION OF DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants enclose herewith a Declaration Under 37 CFR 1.132 (hereafter "Declaration"). The information contained in the Declaration was presented in the Amendment and Request for Reconsideration filed January 21, 2010. Applicants respectfully request that the Examiner consider the information provided in the Declaration, together with the response filed January 21, 2010.

Respectfully submitted,

Hiide YOSHINO et al.

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February 3, 2010

The USPTO is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17, and 1.492, which may be required by this paper to Deposit Account No. 23-0975.

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DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Satoshi Yuki, declare:

That I am a citizen of Japan; and my full post office address is
c/o MITSUBISHI TANABE PHARMA CORPORATION, Tokyo Head Office
2-6, Nihonbashi-Honcho 2-chome, Chuo-ku, Tokyo 103-8405, Japan

That my education and employment history is as follows:

Education
1980 April - 1984 March
College of Biological Sciences, University of Tukuba

Employment
1984 April-
Mitsubishi Yuka Pharmaceuticals
Research Scientist (Pharmacologist)

1986 May-
Department of Neurology, Tohoku University School of Medicine

1988 Jan-
Mitsubishi Kasei Corp.
Research Scientist (Pharmacologist)
Pharmaceuticals Labolatory

1994 Oct-
Mitsubishi Chemical Corp.
Senior Research Scientist (Pharmacologist)
Pharmaceuticals Labo I

1999 Oct-
Mitsubishi-Tokyo Pharmaceuticals Inc.
Senior Research Scientist (Pharmacologist)
Pharmaceuticals Labo I

2001 Oct-
Mitsubishi Pharma Corp.
Senior Research Scientist (Pharmacologist)
Pharmaceuticals Labo II

2007 Oct-
Mitsubishi Tanabe Pharma Corp.
Group Manager/Senior Research Scientist (Pharmacologist)
Pharmacology Department I

That I am familiar with the above-identified application, as well as the Office Action dated August 21, 2009.

That in order to show the novelty and unobviousness of the method claimed in the above-identified application, I have under my control and direction conducted the following experiments. The particulars and results of the experiments are set forth below.

EXPERIMENTAL

The following experiment compares the case where a drug holiday period of 1 day or more is provided once, twice or more (Group A) and the case where such a drug holiday period is not provided (Group B), by using ALS model animal. As demonstrated by the following experimental data, the effect of therapy and/or suppression of progress of ALS or symptoms due to ALS is more excellent in the case where a drug holiday period of 1 day or more is provided once, twice or more (Group A), as compared with the case where such a drug holiday period is not provided (Group B).

Discussion of the Methods

1. Animal

Mutant SOD transgenic rats (J. Neurosci., Dec 2001; 21: 9246-9254), which are used as an ALS model, were used. Genetic analysis was previously carried out, and individuals which are suitable as an ALS model were selected and used for the experiment. (A copy of the reference was submitted with the response filed January 21, 2010.)

Rats which were 20-weeks old (140 days old) were subjected to administration of the drug.

2. Administration of the drug

Group A: For eight individuals, 3-methyl-1-phenyl-2-pyrazoline-5-on (edaravone) (3 mg/kg) was intravenously administered once a day for two days, followed by a drug holiday period of two days, wherein edaravone was not administered. The schedule of drug administration and drug cessation for Group A is shown in the table below.

Day 1	Day 2	Day 3	Day 4
Drug administration	Drug administration	Drug cessation	Drug cessation

Day 5	Day 6	Day 7	Day 8	------
Drug administration	Drug administration	Drug cessation	Drug cessation	-----

This drug administration of two days and drug cessation of two days was repeated until the day before loss of righting reflex.

Group B: For eight individuals, 3-methyl-1-phenyl-2-pyrazoline-5-on (edaravone) (3 mg/kg) was intravenously administered once a day. This drug administration was repeated until the day before loss of righting reflex.

Control Group: For eight individuals, a physiological saline was intravenously administered once a day. This administration was repeated until the day before loss of righting reflex.

3. Evaluation item

The food consumption of one day was measured by measuring the weight of the feeder containing feed by means of a scale for animal.

4. Data processing

For the days after loss of righting reflex, the food consumption of the final measurement day was used.

Discussion of the Results

When ALS proceeds, limb movement disorder and swallowing difficulty occur, and feeding becomes difficult. Therefore, the suppression effect on the reduction of food consumption reflects an effect of therapy and/or suppression of progress of ALS or symptoms due to ALS.

The results of the experiment described above are shown in Fig. 1, which is attached hereto. The measurements were carried out three times a week from 14 days old (20-weeks old) to 250 days old (35-weeks old).

In all of the groups, a reduction of food consumption was observed on or after 26-weeks old

(182 days old). However, the reduction of food consumption in Group A (drug period of two days and drug holiday period of two days) was moderate, and suppression of reduction of food consumption was observed.

Group A showed a significant difference as to the suppression effect of reduction of food consumption on or after 30-weeks old (210 days old), as compared with Group B (daily administration). Accordingly, Group A showed a significantly excellent effect of therapy and/or suppression of progress of ALS or symptoms due to ALS, as compared with Group B.

Conclusion

The total amounts of edaravone administered are different between Groups A and B. Even if the amount of edaravone per single administration is the same, since edaravone is not administered during the drug holiday period, the total amount of edaravone administered in Group A is less than the total amount of edaravone administered in Group B. Nonetheless, Group A showed a more excellent effect as compared with Group B.

One of ordinary skill in the art would generally expect that a more excellent effect would be obtained in the group with a greater total amount of edaravone administered. However, contrary to this expectation, in the claimed invention, even if the total amount of edaravone administered becomes low, the group with the drug holiday period (Group A) showed a more excellent effect than the group of daily administration (Group B). This advantageous effect would not have been expected by one of ordinary skill in the art.

I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

27 Jan 2010
Date

Satoshi Yuki
Signature; Satoshi Yuki